An Amino Acid mixture Mitigates Irradiation Induced gastrointestinal Toxicity

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The Impact of Radiation on the GI Tract

- GI cells receive the most functional damage in the 1st days following irradiation and presents as Acute radiation enteritis.
- Radiation injury leads to dose-dependent nausea, vomiting, diarrhea, and dehydration which are components of acute radiation syndrome.
- Chronic radiation enteritis begins as acute enteritis and may persist months to years after therapy.
- Early supportive care limits acute and chronic radiation enteritis.
Why Target the Small Intestine?

~80% of fluid absorption occurs in the small intestine
Chloride Secretion Occurs in the Crypt and produces diarrhea
Electrolyte & Fluid Absorption Occurs in Villus
NHE-3 protein levels correlated with decreased in Na⁺ and Cl⁻ fluxes

NHE-3 is decreased at doses as low as 1 Gy

85 kDa
β actin

NHE-3 protein levels correlated with decreased in Na⁺ and Cl⁻ fluxes
Radiation Results in Significant Anion Secretion

Radiation-induced anion secretion leads to diarrhea

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Enterade-r Decreases Chloride Secretion and Diarrhea

Irradiation

Irradiation + Enterade-R

Cl Flux ($\mu$eq.cm$^{-2}$h$^{-1}$)
Bicarbonate secretion is essential for neutralizing the acid emptied into the duodenum during regular gastric emptying.

Reduced HCO₃⁻ secretion can result in an acid peptic disease-like condition.

Nausea and vomiting are common.
Enterade-r decreases nausea and vomiting.
Radiation Decreases Glucose Absorption

- Graph showing the change in glucose absorption ($\Delta I_{sc}$) with different radiation doses (0 Gy, 1 Gy, 3 Gy, 5 Gy, 7 Gy).
- Bar graph with error bars.
- Line graph showing Vmax and Km values for various radiation doses.

- Vmax values decrease with increasing radiation dose.
- Km values increase with increasing radiation dose.
Radiation Increases Lysine Absorption

\( \Delta I_{sc} \) (\( \mu \text{A/cm}^2 \))

- 0 Gy
- 1 Gy
- 3 Gy
- 5 Gy
- 7 Gy

Lysine
Radiation Decreases Glutamine Absorption

Graph showing the change in glutamine absorption ($\Delta J_{sc}$) in microamperes per square centimeter ($\mu$A/cm$^2$) with different doses of radiation: 0 Gy (black), 1 Gy (red), 3 Gy (blue), 5 Gy (magenta), and 7 Gy (green). Each bar represents the mean with error bars indicating variability.
The Effects of Radiation Enteritis

- Decreases Na absorption
- Increases Cl secretion
- Decreases HCO₃ secretion in the upper GI
- Increases the secretory effects of glucose and certain amino acids
- Increases paracellular permeability
AA Cocktail Increases Sodium Selectivity in 0-Gy and 5-Gy Mice
Enterade-R Decreases Plasma Endotoxin and IL-1β
Enterade-R Decreases Weight Loss and Increases Survival

Body Weight

Survival Studies

- **Survival rate (%)**
  - Days: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18
  - Survival rate: 0%, 20%, 40%, 60%, 80%, 100%

- **Residual body weight (%)**
  - Days: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18
  - Residual body weight: 100%, 95%, 90%, 85%, 80%
Why Does Enterade-r Help?

✧ Relies on a functional approach to correct nutrient and electrolyte imbalances
✧ Decreases osmotic diarrhea
✧ Restores epithelial barrier function
✧ Decreases morbidity associated with radiation
✧ Increases survival following irradiation
Enterade-r can be used to mitigate acute radiation enteritis when given orally within the first week following radiation exposure.

The agent is safe at doses below the GI syndrome level (“worried well”).

Patients include men, women, children, and pregnant women.

Enterade-r does not reduce the benefits of other therapies for comorbid disease.

Enterade-r can be used in combination with other radiation mitigation agents.
Questions ?
What is Enterade-r?

- A medical food that mitigates gastrointestinal toxicity and is targeted at patients receiving radiotherapy and chemotherapy.

- A selection of amino acids and electrolytes at the optimal pH and osmolarity for distressed gastrointestinal function.
Transepithelial electrolyte movement studied using unidirectional (Jms & Jsm) and net flux of Cl\(^-\) and Na\(^+\) (Jnet = Jms - Jsm) using \(^{36}\)Cl and \(^{22}\)Na (CPM2 - CPM1 - Blank) / 9/10 x 5 x 4 x 140 (CPM Hot - Blank) x 10 x 0.3.
Glucose Stimulates Sodium Absorption

Na flux (µEq.h⁻¹.cm⁻²)

Basal  Glucose
Glucose Stimulates Anion Secretion

![Graph showing the effect of glucose on Cl- secretion](image)